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POSTER SESSION

1026 Safety and Efficacy of Drug Therapy of Coronary Artery Disease

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: Noon-1:00 p.m.

1026-100 Effect of Roxithromycin on Clinical Cardiovascular Events in Patients Undergoing Coronary Angioplasty

Jan Kaehler, Antje Haar, Klaus-Peter Schaps, Marion Carstensen, Ralf Koester, Wolfram Terres, Thomas Meinertz, University Hospital Hamburg, Hamburg, Germany, Celle General Hospital, Celle, Germany

Background: Seropositivity for chlamydia pneumoniae has been associated with coronary artery disease, but results of interventional studies with antibiotics have been contradictory. We therefore investigated whether clinical cardiovascular events in patients undergoing coronary angioplasty can be reduced by medication with roxithromycin.
Methods: 327 consecutive patients undergoing coronary angioplasty were randomized to roxithromycin 300 mg/d for 6 weeks or placebo regardless of antibody titers. The primary clinical end point included cardiovascular death, nonfatal infarction (MI) and symptomatic restenosis at 1 year. Indication for angioplasty was stable angina in 51/47% of patients (roxithromycin/placebo), unstable angina in 43/44% and prognostic in 6/7% of patients.
Results: Treatment groups were balanced for age, BMI and risk factors, and roxithromycin was well tolerated. During the trial period of 1 year, 36 endpoints occurred (cardiovascular death, 1; MI, 4; and symptomatic restenosis, 31), with 20 events in the roxithromycin group and 16 in the placebo group, n.s.. When analyzed for the 3 indication groups, there was a trend towards more events in the unstable angina group receiving roxithromycin, but no significant differences could be detected in any of the groups. Ischemic stroke occurred in 3 roxithromycin vs. 0 placebo patients, n.s..
Conclusion: The results of our study suggest that antibiotic therapy with roxithromycin in unselected patients undergoing coronary angioplasty is not associated with a reduction of clinical cardiovascular events. However, this does not exclude positive effects of antibiotics in subgroups such as patients with high antibody titers against chlamydia pneumoniae.

1026-101 Low-Molecular-Weight Heparin Alone and With IIb/IIIa Inhibitors in Patients With Renal Failure and Non-ST Elevation Acute Coronary Syndromes: Insights From the Global Registry of Acute Coronary Events

Jean-Philippe Collet, Giancarlo Agnelli, Frans J. Van de Werf, David Brieger, Enrique P. Gurfinkel, Jose Lopez-Sendon, Neelam Gowda, Gilles Montalescot, on behalf of the GRACE Investigators, Hôpital Pitié-Salpétrière, Paris, France, University of Perugia - Ospedale Silvestrini, Perugia, Italy

Background: LMWH is a reference treatment for NSTE-ACS. Data are lacking in patients (pts) with moderate (creatinine clearance [CC] >30-≤60 mL/min, MRF) & severe (≤30, SRF) renal failure.
Hypothesis: LMWH alone or with IIb/IIIa inhibitors provides greater benefit than unfractionated heparin (UFH) irrespective of renal status.
Methods: Data were utilized from 13,325 NSTE-ACS pts.
Results: Pts with MRF (n=3,049) or SRF (n=816) were at higher risk of adverse outcomes than normal renal function (NRF) pts as reflected by an increased prevalence of elderly pts, diabetes, heart failure, ST depression & positive troponin. Decreasing CC was an independent predictor of death at 30 d (OR 1.8/30 mL/min) & hospital major bleeding (OR 1.3/30 mL/min). While 50% of pts were treated with LMWH (84% enoxaparin), there was significantly less use of LMWH+IIb/IIIa in MRF (15%) & SRF (12%) than NRF pts (21%). The magnitude of benefit of LMWH alone over UFH alone was similar irrespective of renal status (Table). Use of LMWH alone was an independent predictor of survival (OR 0.57) and less bleeding (OR 0.54). Bleeding rates were lower with LMWH+IIb/IIIa compared to UFH+IIb/IIIa irrespective of renal status. UFH+IIb/IIIa was an independent predictor of bleeding (OR 2.12).

CC (mL/min)	≤30	30-60	>60	P-value
Death				
UFH (%)	43 (26)	66 (12)	47 (5)	<0.0001
LMWH (%)	38 (22)	48 (8)	31 (3)	<0.0001
LMWH vs UFH (P-value)	0.30	0.018	0.015	
Major Bleeding				
UFH (%)	18 (8)	35 (4)	31 (2)	<0.0001
LMWH (%)	13 (5)	15 (2)	5 (1)	<0.0001
UFH vs LMWH (P-value)	0.27	0.0008	0.002	

Conclusion: In this observational study renal failure is associated with an excess of cardiovascular death & major bleeding. Bleeding complications are more frequent & severe, & outcomes apparently worse, in patients treated with UFH than with those on LMWH.

1026-102 Efficacy and Safety of a Chronotherapeutic Graded-Release Diltiazem Hydrochloride Formulation Dosed at Bedtime Compared to Placebo and to Morning Dosing in Chronic Stable Angina Pectoris

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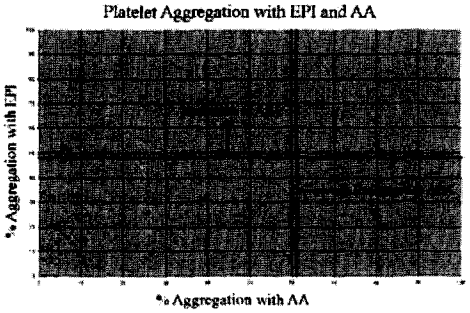
Background: The efficacy and safety of a chronotherapeutic graded-release diltiazem HCl formulation (GRD) dosed once-daily at 10 PM in doses of 180, 360 and 420 mg were evaluated in a 3-week multi-center, randomized, double-blind, parallel group trial by comparison to placebo and to GRD 360 mg dosed once-daily at 8 AM in patients (n=311) with chronic stable angina pectoris.
Methods: Standard Bruce protocol treadmill stress test was performed at baseline and endpoint, between 6 – 8 PM (trough for PM doses) and between 7 – 11 AM (trough for AM doses). Efficacy variables were change from baseline in total duration of exercise (primary); and time to onset of angina and time to ≥1 mm ST segment depression (secondary variables).
Results: All PM doses of GRD showed a significant ($p<0.03$) increase in the total duration of exercise at trough compared to placebo, with the 360 PM dose showing the greatest increase. In contrast, GRD 360 AM showed an increase in the total duration of exercise at trough that was not significant ($p=0.06$) compared to placebo AM. Between 7 – 11 AM, all PM doses showed significantly greater increase ($p\leq0.0002$) in the total duration of exercise versus placebo. GRD 360 PM showed a 4-fold improvement over placebo compared to GRD 360 AM. Time to onset of angina was significantly increased for all GRD PM doses compared to placebo between 6 – 8 PM ($p<0.02$) and between 7 – 11 AM ($p<0.03$). Only the 360 PM dose showed a significant ($p<0.03$) increase in time to onset of myocardial ischemia between 6 – 8 PM, but between 7 – 11 AM all GRD PM doses showed a significant increase compared to placebo ($p<0.03$). Overall, the incidence of adverse events (AEs) for all GRD groups combined (42.4%) was less than that obtained for the placebo group (47.5%). Improvement in exercise tolerance from 180 to 360 PM occurred without an associated increase in AEs compared to placebo.
Conclusion: Bedtime GRD significantly increased exercise tolerance in patients with angina pectoris over the 24-hour dosing interval. A greater 4-fold improvement versus placebo in exercise tolerance occurred between 7 – 11 AM for the PM dose compared to the same AM dose, coinciding with the period of clustering of cardiovascular events. GRD was safe and very well tolerated.

1026-103 Aspirin Resistance in Patients With Coronary Artery Disease

Brian L. Walton Andrew B. Civitello, James M. Wilson, Paul Allison, Arthur Bracey, James J. Ferguson, St. Luke's Episcopal Hospital/Texas Heart Institute, Houston, TX

Background: Standard of care for the treatment of patients with coronary artery disease (CAD) includes antiplatelet therapy with aspirin (ASA). However, the antiplatelet effect of ASA varies across the broad distribution of CAD patients. Aspirin resistance refers to a cohort of patients that do not achieve significant inhibition of platelet aggregation with ASA therapy. Assessment of the true prevalence of aspirin resistance is complicated by lack of a uniform definition; moreover, the clinical implications ASA resistance is unknown. This study evaluates the prevalence of aspirin resistance and the spectrum of responsiveness to ASA therapy.
Methods: Patients with CAD who were treated with aspirin (81-325 mg) for seven consecutive days underwent platelet aggregometry (PA). Standard PA using 0.5 mg/ml arachidonic acid (AA) and 1 x 10^{-4} M epinephrine (EPI) as agonists was performed and reported as percentage aggregation. Normal thresholds for platelet responsiveness without ASA were defined as 48% aggregation for EPI and 63 % aggregation for AA.
Results: 48 patients including 6 (12.5%) females and 42 (87.5%) males were studied. One patient (2%) was overtly aspirin resistant, defined as abnormal response to both agonists. 8 patients (16.7%) demonstrated partial response to ASA, with an abnormal response to one agonist and a normal response to the other agonist.



Conclusion: A significant portion of patients (18.8%) with CAD have complete or partial resistance to ASA therapy using platelet aggregometry.